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Calcified Tumors of the Ovary

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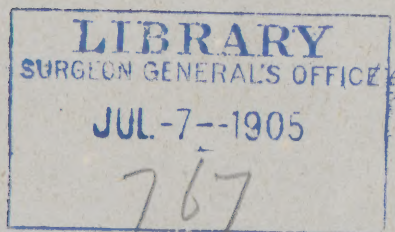
(With two illustrations)

REPRINTED FROM

THE AMERICAN JOURNAL OF OBSTETRICS
Vol. XXVIII., No. 1, 1893

NEW YORK

WILLIAM WOOD & COMPANY, PUBLISHERS
1893



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CALCIFIED TUMORS OF THE OVARY.¹

WITHIN the past year several gentlemen have sent us solid tumors of the ovary which they supposed were of osseous nature, but on careful microscopical examination we found that they were not composed of bone, but were due to the calcification of ovarian structures, with which we are all familiar. In several instances the tumors were supposed to be osteomata of the ovary, when in reality they were simply calcified fibromata; and in another case what was considered as a nodule of true bone was found to be a calcified corpus luteum.

We have carefully considered the literature on the subject, and find that very little is known concerning calcific changes in the ovary, and that no one has attempted to collect even the little which is known about them. Such being the case, we have thought that it might be of interest to bring before you the specimens which have come into our hands, and then to consider what we know of this variety of changes in the ovary.

CASE I. *Calcified Fibromata of both Ovaries.*—These specimens we owe to the courtesy of Dr. Copeland, of Milwaukee, who sent them to us with the statement that they had been examined by a pathologist, who reported that they were osteomata of the ovary.

The following is an abstract of Dr. Copeland's history of the case: Age 28, married five years; no children. Menses regu-

¹ From the Pathological Laboratory of the Johns Hopkins University and Hospital. Read before the American Gynecological Society, May, 1893.

lar, of four days' duration, and painful. Last year had an attack of cramp-like pains in the lower part of the abdomen, and during the past year has had occasional attacks of frequent micturition and has felt a lump in the right ovarian region. Two weeks before Dr. Copeland saw her she fell down-stairs. The next day, one week before the expected menstrual period, she had a profuse flow of blood, which weakened her considerably and led her to consult a physician. On examination a hard tumor was found on the right of the uterus. Laparotomy; removal of both tubes and ovaries; prompt recovery.

Description of Specimens.—The specimens were hardened in alcohol, and consisted of the appendages from each side, those from the right side being in several pieces. Left side: The tube is 8 cm. in length and 0.4 and 0.6 cm. at its thinnest and thickest parts, and is apparently normal. The parovarium is intact. The ovary measures 5, 3, and 1.75 cm. in its various diameters. On its surface are many cicatrices, but no adhesions. On section its median end is found to be occupied by a hard, roundish nodule, 12, 16, and 18 mm. in its various diameters, which lies in an apparent capsule, with which it is connected by numerous connective-tissue bands. On sawing through the nodule, which is of bony hardness, its cut surface is seen to present a mottled appearance and the general color of bone. At the lateral end of the ovary are seen the corrugated walls of an old corpus luteum about 13 mm. in diameter. Here and there are seen several follicles with clotted contents. Right side: The tube is 7 cm. in length and 0.4 and 0.6 cm. at its thinnest and thickest parts, and is apparently normal. The parovarium is intact. The ovary may be reconstructed from the various portions, when it is apparent that a large, hard nodule, measuring 7, 6, and 5 cm. in its various diameters, arose from its median end, for its lateral end is practically intact, presenting at one point a corpus luteum 1 by 0.5 cm.

From the anterior and interior surface of the ovary arise a number of small, pedunculated fibromata, the largest being 6 mm. in diameter. From the neighborhood of these small fibromata the ovarian tissue which covers the hard nodule begins to decrease in thickness, and soon becomes as thin as a sheet of paper. This thin covering is perforated in a number of places, through which the surface of the hard mass is visible.

The hard mass¹ weighs two hundred and twenty grammes and is extremely hard, almost resembling ivory in its general consistence. When thrown upon a hard surface it rebounds like a billiard ball. On section its surface is mottled and is similar to that of the smaller nodule in the left ovary.

Microscopical Examination.—Dry sections from both masses show no trace of bony structure. Portions of the masses from each ovary were decalcified by a ten-per-cent solution of nitric acid, when microscopic sections could readily be made. Stained sections show that the masses from both ovaries are absolutely identical in structure. They are composed of typical fibrous tissue, made up of bundles of dense connective tissue, which interlace in all directions, with very few long nuclei. This tissue stains readily and is more or less similar to that found in the hilum of the ovary, except that it is much poorer in blood vessels and contains many more veins than arteries. Scattered all through it are irregularly shaped areas of various size, which stain deeply with hematoxylin. Generally they have very sharply marked contours and in their interior show signs of striation, but no trace of nuclei can be found within them. They represent areas of calcification from which the lime salts have been dissolved by the nitric acid. (Their appearance is fairly well represented in Fig. 1, which is drawn under a low power.) Under the high power of the microscope the development of the calcified areas may be clearly traced. Here and there we see individual cells which have lost their nuclei and present the typical appearance of coagulation necrosis. Then we see similar cells which contain perhaps only a single calcareous granule, and others which are entirely calcified. By the coalescence of individual calcified cells larger calcified masses are produced; these in turn coalesce with others and form the large areas shown in Fig. 1.

It is evident that the calcification has occurred in necrotic areas of the fibroma. Nowhere in the specimen is there any trace whatever of bone. Except for the calcified fibromata, both the tubes and ovaries are normal.

¹ Chemical analysis of the mass shows that it contains moisture, 8.40 per cent; agaric matter, 21.36 per cent; and mineral matter, 68.24 per cent. The mineral matter consists of the phosphates and carbonates of calcium in the proportion of fifteen to one, and a trace of sodium phosphate.

CASE II. *Calcified Fibroma of the Left Ovary.*—We are indebted to Dr. Robt. T. Wilson, of Baltimore, for the following specimen. The history is as follows : Age 24, single ; menses first appeared at 13 years ; has suffered more or less ever since their appearance. For the past three years menses every six to seven weeks, lasting five to seven days, confining her to bed during the entire period, and not infrequently are accompanied by con-

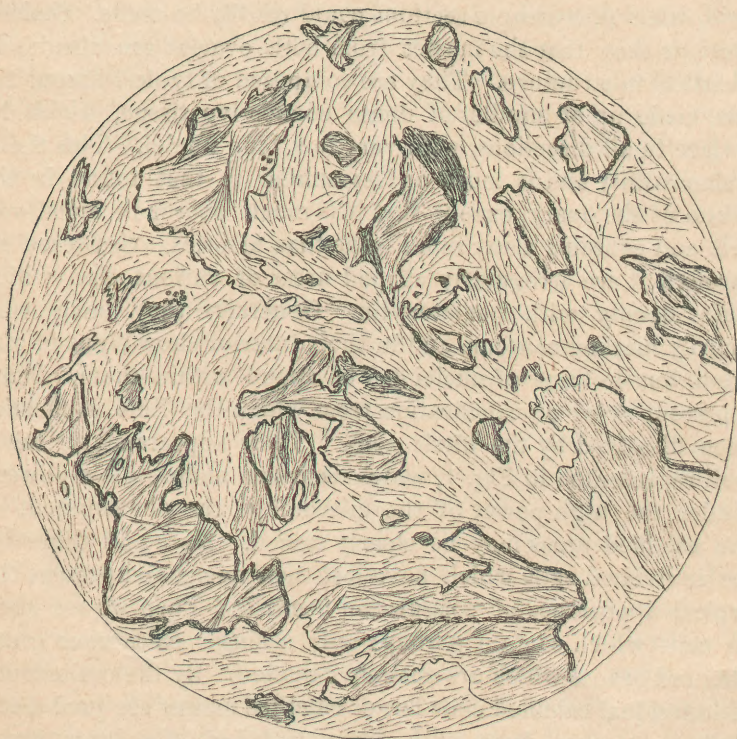


FIG. 1.—Calcified fibroma of ovary, Case 1. (Zeiss objective AA. Eye piece No. 4.)

vulsions. For the three months previous to operation severe pains in back and ovarian regions, constant headache and insomnia, which necessitated the frequent employment of morphia. Three or four weeks before the operation she is said to have had an attack of peritonitis.

Upon examination the "left ovary was found enlarged and prolapsed." Laparotomy ; removal of both tubes and ovaries.

At operation "the peritoneum was found thickened, showing signs of chronic inflammation." Death on the seventh day from peritonitis.

Description of Specimens.—Left side: The tube is 9 cm. in length and 0.3 and 0.4 cm. in diameter at its thickest and thinnest parts, and is apparently normal. The parovarium is intact. The ovary measures 5, 4, and 4 cm. in its various diameters, and is very hard to the touch. On its superior margin is a fresh corpus luteum, 2 by 0.75 cm., filled with decolorized clot; its yellow margins are 1 mm. thick. The surface of the ovary is glistening and presents numerous rounded elevations which vary from 1 to 10 mm. in diameter. The entire ovary is hard to the touch, and when dropped upon the table sounds as if it were bone. It is impossible to cut it with a knife, for it is found that its greater part is composed of a hard mass which is probably calcareous. The mass is entirely covered by typical ovarian tissue, which varies from $\frac{1}{2}$ to 3 mm. in thickness and contains both follicles and the yellow remains of an old corpus luteum. The greater number of the nodules noted on the exterior of the ovary are found to correspond to irregularities upon the outer surface of the hard mass, and are thoroughly calcified; several of them, however, particularly one on the posterior surface, are readily cut and present the usual appearance of fibromata. On the anterior surface of the ovary several of these calcareous nodules project through the ovarian tissue which covers the rest of the mass. The mass can be cut only by means of a saw, and on section it is seen to be composed of a number of small, very hard areas separated by bands of tissue. The fibrous mass on the posterior surface, mentioned above, is seen to be continuous with the main portion of the hard mass. Right side: The tube is 9.5 cm. in length and 0.3 and 0.5 cm. in diameter at its thinnest and thickest parts, and is apparently normal. The ovary measures 3, 2.5, and 1.5 cm. in its various diameters, with many corrugations, but no adhesions on its surface. On section it contains many follicles and corpora fibrosa.

Microscopic Examination.—Both tubes are perfectly normal. Sections from decalcified portions of the left ovary show that the great part of the tumor is composed of interlacing bands of connective tissue, with numerous irregularly shaped areas of

calcification of various size scattered through it. No definite structure can be made out in the calcified areas; they present a somewhat striated appearance, with absolutely no trace of nuclei. The growth, except for the calcified areas, resembles the tissue usually found in the hilum of the ovary, except that it contains fewer blood vessels; a considerable number of veins may be made out, but only a very small proportion of arteries. It is readily seen that the tumor is identical with those in the preceding case, and that Fig. 1 applies equally well to it. The ovarian tissue surrounding the tumor mass presents its usual appearance and contains ova, follicles, corpora lutea, and corpora fibrosa. In one corpus fibrosum there is a small cavity, apparently indicating the formation of a small cyst. Except for a slight amount of endarteritis, the right ovary is normal.

From the description of the microscopical appearance of these three tumors there can be absolutely no doubt as to their nature. A single glance at Fig. 1—which applies equally to all of them, for they all present identically the same structure—suffices to show that all the characteristics of bone formation are lacking and that we have to deal with the calcification of necrotic areas in ovarian fibroids.

That the calcification is the sequel of necrosis has already been indicated, and will be made perfectly clear when we come to consider the etiology of calcification.

A point of considerable interest in all of these tumors is the fact that the function of the small portions of unchanged ovarian tissue by which the tumors are surrounded is not interfered with by the formation and growth of the fibromata and their subsequent calcification, as is shown by the fact that typical corpora lutea may be seen in each of the three ovaries.

The fact that we have shown that the tumors under consideration are not osteomata of the ovary does not take away at all from their interest; for a careful survey of the literature shows that calcified fibromata of the ovary are of extremely rare occurrence, and, if for no other reason, are of interest on account of their rarity. It is well known that uncomplicated fibromata of the ovary occur but rarely, as is stated by Leopold,¹⁹ Olshausen,³² and Coe,⁶ and that probably the great majority of cases so described are in reality sarcomata. If the ovarian fibromata them-

¹⁹ The small figures refer to Bibliography at end of the article.

selves are rare, how much more so must they be when calcified!

A considerable number of writers state that ovarian fibroids do occasionally become calcified. They usually base their statements upon the analogy which should exist between fibroids of the ovary and uterus; for it is well known that calcified areas are not infrequently found in uterine fibromata and myofibromata, but they have not seen such cases themselves. In this connection may be mentioned Hooper,¹² Klob,¹⁷ Ashwell,³ Churchill,⁴ Talamon,⁴² and Howell.¹³

As far as we can learn, the only case which is without doubt similar to ours is one reported in 1859 by Sir Spencer Wells.⁴⁶ At the autopsy on a woman, age 64, "dead of diseased heart and kidneys," he found a tumor, the size of a cocoanut, occupying the seat of the left ovary. It was so hard that it had to be cut with a saw, and on microscopic examination it was seen to be "composed of fibrous tissue, the denser parts being calcified by a deposit of carbonate of lime. There was no tissue found in the least resembling bone."

As our three tumors were considered to be of a bony character until a careful microscopic examination demonstrated that they were calcified fibromata, we do not consider that we shall go far wrong if we assume that all of the so-called bony tumors of the ovary which have hitherto been described, and in which nothing definite is said as to their microscopic appearance, are likewise calcified, and not osseous, tumors of the ovary. For it is well known what great confusion has long existed as to the significance of the terms calcification, petrification, and ossification, and the practical impossibility of distinguishing between them except by means of the microscope, even when one holds the most approved views as to the difference between the several processes.

From this standpoint the number of these cases may be considerably increased, and it is curious that more was said about them by the writers of seventy-five or one hundred years ago than by those of more recent times. The first case of this variety of which we are able to find any record is one reported by Schlenker³⁸ in a thesis entitled "*De singulari Ovarii sinistri Morbo.*" A few years later (1760) Le Clerc de Beaucoudray,³ in an article entitled "*Sur un Ovaire ossifié,*" gave a meagre description of a case with which he had met at autopsy.

That a considerable number of cases had been described during the past century is evident from the statement of Voigtel¹⁵ in his work on pathological anatomy (1805), who referred to several bony tumors of the ovary and stated "that one not infrequently finds stony concretions in the ovaries." Unfortunately, however, in most cases we have been unable to verify his statements by recourse to the original articles; for many of them could not be found in the Library of the Surgeon-General's Office in Washington, and in several instances his references were faulty.

Haase¹¹ (1836) referred to an ossified tumor of the ovary which had been presented to the Entbindungs-Institut in Dresden by Dr. Rotter. It measured 3, 4, and 5 inches in its various diameters, and weighed eight ounces. He said that "the mass is composed of almost bony nodules the size of peas, which are connected and grouped together."

Löbl²² (1844) also described a case of Rokitansky's as follows: "An ossified fibroid the size of a child's head, with numerous flattish bosses, was attached to the external end of the right ovary and elongated it and its ligament to a considerable extent."

There can be but little doubt that an ovarian tumor which constituted an obstacle to labor in a woman upon whom Kleinwächter¹⁶ was obliged to perform Cesarean section, was also a calcified fibroma. In this case the right ovary was converted into a tumor the size of a child's head, which filled up the pelvis and was removed at autopsy. "It was rounded, nodulated, and hard, and, with the exception of a portion the size of a walnut, was entirely ossified. The portion which was not ossified creaked on section, had a white, firm, fibrous structure, and on microscopical examination was a simple fibroid."

The same may be said of a "bony tumor" removed by Nottingham²¹ in 1872 from a woman aged 25. The tumor occupied the entire right ovary and was as large as a fetal head. He says that it was "encased in a tegumentary envelope, it was almost entirely bone, there being here and there a slight admixture of fibrous substance. Its osseous nature was so decided that a strong knife could not be made to penetrate it at any point. To open it for inspection a saw had to be brought into requisition. Its weight, when dried of blood, was one and three-quarter pounds. Neither hair nor teeth were observed in any part of it."

The only other reference to a calcified tumor of the ovary which we have been able to find is a case reported to the New York Obstetrical Society by our Fellow, Dr. H. M. Sims³² (1889), who, on removing the ovaries for the cure of a uterine fibroid, found that the right ovary "was calcified and hardened." But as he failed to give any particulars concerning the specimen, it is doubtful whether it belongs in this category.

When we consider that in the literature for the past one hundred and fifty years we have been able to find only eight cases which can be compared with those which we have just described, and that several of these eight cases are open to serious doubt, it is evident how very rare calcified fibromata of the ovary must be.

True, osseous tumors may also occur in the ovary, but they are even more rare than calcified tumors, and it is far more difficult to give a satisfactory explanation for their occurrence than for the calcific changes in fibromata. And it must also be remembered that osseous formations occur but rarely in any portion of the body, while calcification occurs very frequently in many organs. Of course, in speaking of osseous tumors of the ovary, we must exclude all growths which are connected with dermoid cysts, and consider only those in which we find no other deviation from the normal structure of the ovary than the new bone formation. Osseous formations of this character can only be explained by Cohnheim's tumor hypothesis.

The only cases of osseous formations in the ovary are those mentioned by Fürst,¹⁰ Reiss,³⁴ Waldeyer,⁴⁴ and Winckel.⁴⁷ In the case of Fürst and the one mentioned by Winckel, the osseous formation occurred in the walls of ovarian cysts, so that they can hardly be considered in this connection. Reiss' case was a fibroma of the ovary, which at its lateral end presented a number of areas composed of hyaline cartilage, in the midst of which was a nodule, the size of a cherry, which macroscopically presented the appearance of spongy bone, which it was found to be upon microscopic examination. This, however, would appear rather as a further development of the enchondroma than as an osseous tumor of the ovary.

Accordingly the only tumor which might have been confounded with the calcified fibromata of which we have been speaking is the one reported by Waldeyer⁴⁴ under the title,

"Diffuse Fibroid of the Ovary of a Peculiar Structure" ("Diffuses Eierstocksfibrom von eigenthümlichem Baue"). This was a very hard tumor, measuring 15, 11, and 9 cm. in its various diameters, which macroscopically presented the appearance of an osteoid tumor, recalling those from the upper jaw. But its microscopic appearance did not justify him in concluding that it was true bone. Admitting, however, that the case described by Waldeyer⁴⁴ was really an osteoma—for typical osteomata have been described in the testicle (Neumann³⁰), and there is no reason why they should not also occur in the ovary—it is seen that the literature affords only a single case (and that a doubtful one) of an osseous growth of the ovary which can be compared with the calcified fibromata under consideration.

In view of the facts here brought forward, we believe that it is perfectly justifiable to consider that any solid tumor of the ovary is a calcified fibroma, even if at first sight it presents all the characteristics of bone, unless a microscopic examination by a competent observer demonstrates that it is really an osteoma.

CASE III. *Calcified Corpus Luteum*.—The specimen which we now present was exhibited last year at the New York Obstetrical Society by our distinguished Fellow, Dr. Coe,⁵ as a "diseased ovary containing true bone, and not being a dermoid cyst," after which he sent it to us. It was removed from an unmarried woman, who suffered severely with her menses, especially over the region of the right ovary. At the operation both tubes and ovaries were removed. The left ovary was cystic and enlarged to the size of a Messina orange, the right was the size of a walnut; both tubes were normal, and the uterus small, retroflexed, and non-adherent. In the centre of the right ovary was the nodule, which we shall describe, and which was pronounced by a New York pathologist to "consist of true bone, while in its centre was a soft mass presenting the microscopical appearance of marrow."

Description of Specimen.—Left tube and ovary preserved in alcohol. The tube is 6 cm. in length and 0.3 and 0.5 cm. in diameter at its thinnest and thickest parts. It is apparently normal, as is also the parovarium. The ovary has been split open and is 5 cm. long and 2.5 cm. deep. On its surface are many cicatrices, but no signs of adhesions. In its centre is a

hard mass, 12 mm. in diameter, of bone-like consistence. When sawed through it is seen to consist of two portions, a soft, pinkish central portion (Fig. 2 B), and a hard, bone-like exterior (Fig. 2 A) which is 2 mm. thick and of a distinctly yellow color. The central portion of the nodule resembles partially organized blood clot. The rest of the ovary presents a normal appearance.

Microscopic Examination.—After decalcification of a portion of the nodule, sections are readily cut. Neither the examination of thin portions of the nodule in its natural state, nor the examination of stained sections after decalcification, shows any signs of osseous structure.

The decalcified sections, in general, stain poorly ; but the hard exterior of the nodule stains readily with hematoxylin, and presents a more or less homogeneous granular appearance, in which it is impossible to distinguish any sign of nuclei. This is surrounded by more or less typical ovarian stroma which stains

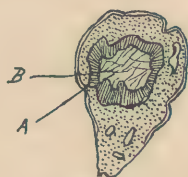


FIG. 2.—Cross-section right ovary, Case 3, natural size, showing calcified corpus luteum. A, calcified outer margin; B, soft tissue in centre.

poorly. The soft central portion of the nodule is composed of dense fibrous tissue which is very poor in cells. Between this and the decalcified portion we see several layers of small cells, which possibly correspond to the membrana granulosa, though it is impossible to state their origin with certainty. In the ovarian stroma surrounding the decalcified nodule are numerous round, stellate crystals, which are probably the result of the decalcification. In all probability the specimen represents a calcification of the large cells which surround a ripe Graafian follicle, and which form the yellow margin of the corpus luteum, while the fibrous tissue in its interior probably represents an organized blood clot.

After our examination Dr. Coe withdrew the statement that the nodule was composed of bone, and upon the strength of it Bland Sutton,⁴¹ in December last, reported two cases of calcified

corpora lutea with which he had met. In one case there were two calcified corpora lutea in the same ovary, and in the second case there was a single one which measured 3 by 1 cm. All three of his calcified corpora lutea were of a bright-yellow color and consisted of a dense tissue in which lime salts were deposited.

When we first examined our specimen of calcified corpus luteum we believed that we had found something absolutely unique. But this supposition was, of course, proved to be without foundation by the publication of Sutton's⁴¹ cases; and a search through the literature showed that a number of the older writers had met with similar conditions, which, in some instances, they had interpreted correctly, while in other cases their excellent objective descriptions leave but little doubt that they had to deal with similar bodies. Thus Morgagni^{24 25 26} recorded three cases in which it is more than likely that he had to deal with various forms of calcified corpora lutea. Of one case he said:²⁴ "In the other ovary, besides the smaller vesicles filled with clear fluid, I have found larger cellules (cellulas), and two of them empty, one of which had a partly osseous tunic, while the other was entirely osseous and marked by so many sulci that it resembled the folds of the intestine." In a second case he said:²⁵ "In the same ovary in which there was the corpus luteum there was a rounded osseous mass (cellula) whose centre was filled with a bloody fluid." And in a third case, occurring in a woman aged 50:²⁶ "The ovaries were not only white, hard, and uneven, but hidden in the centre of one of them is a white body, rounded, almost entirely hollow, and cartilaginous." More or less similar cases have also been reported by Sandifort³⁷ and Walter.⁴⁵ And Rokitansky³⁵ reported a case of which there can be no doubt. In this there was an old corpus luteum the size of a nut, in whose wall at one point there was a hard, osseous (?) nodule the size of a pea. And Klob¹⁷ stated that Meckel²³ said that "shrivelled-up corpora albida become ossified and occasionally are converted into solid bone."

It is thus readily seen that the observations of Sutton⁴¹ and ourselves are not isolated, and other observers have also met with calcified corpora lutea.

Indeed, upon consideration, it is surprising that more cases have not been observed and reported; for it will soon be shown

that the corpus luteum frequently presents conditions which apparently should predispose it to calcification.

Etiology.—Having described the cases of calcified tumors of the ovary with which we have met, and given some idea as to the literature upon the subject, we propose to consider for a few moments the general etiology of calcification, and then attempt to explain why the tumors under consideration should have become calcified.

It is needless to dwell upon the frequent occurrence of calcification in the various organs, and it will suffice to state that calcareous deposits occur very frequently in the blood vessels, lungs, tumors of various kinds (especially fibromata and myomata), kidneys, and also in foreign bodies, as in the fetus of extra-uterine pregnancy, forming the lithopedion, and in various forms of parasites. And in all these conditions the calcification is more or less of a conservative process, as is most clearly illustrated by the foci of calcification which are found in the lungs after the healing of tuberculosis.

Of course there must be some general reason why calcification should occur in the various tissues as frequently as it does, and this is to be found in the fact that the process is nearly always preceded by more or less necrosis of the affected parts. By this it is not meant that all forms of necrosis lead to calcification, for it is well known that such is not the case; but calcification only follows certain varieties of necrosis, particularly coagulation necrosis (Cohnheim⁷ and Litten²¹), and then only under certain conditions.

These conditions are best studied in experiments upon the lower animals, and especially upon the kidneys of rabbits. It is now a well-established fact, as was first pointed out by Saikowsky,²⁶ that calcareous material is deposited in the kidneys of rabbits which have been poisoned with corrosive sublimate. Saikowsky's results have been confirmed by a large number of investigators, but especially by Kaufmann,¹⁶ Neuberger,²⁸ and others. In these cases the calcareous material appears in the kidneys within twenty-four hours after the sublimate has been given, and gradually increases in amount, if the animal survives long enough, until the kidney is almost too hard to be cut with a knife. It has been clearly shown that the first effect of the sublimate upon the kidneys is to produce coagulation necrosis of its epithelium, especially in the convoluted tubules, in which

the lime salts are soon deposited. Strange to say, the same deposit of calcareous material does not occur in dogs when poisoned with sublimate; but in them it is found that the renal epithelium undergoes fatty degeneration instead of coagulation necrosis, and calcification does not appear to follow that variety of degeneration.

Calcareous changes exactly similar to those observed in rabbits occur in women who have died from sublimate poisoning, and have been described by Dahl,⁸ Fleischmann,⁹ Kaufmann,¹⁵ Netzel,²⁷ Prévost,³³ Steffek,⁴⁰ and Virchow.

Poisoning with other substances also leads to renal changes similar to those produced by sublimate. Among them may be mentioned poisoning with glycerin and pyrogallie acid (Afanassiew¹), bismuth (Langbans¹⁶), aloin and phosphorus (Neuberger²⁹). And the calcareous deposits which occasionally follow diphtheria and scarlet fever have been attributed by Litten²¹ to the necrotic changes which are produced in the kidneys by the poisons accompanying the diseases.

In all these instances the first effect of the poison is to produce coagulation necrosis of the renal epithelium, particularly in the convoluted tubules.

Litten,²⁰ in his beautiful experimental work upon the production of infarctions, found that arterial anemia would produce almost identically the same changes. Thus, after ligating the renal artery for two hours and then removing the ligature, no changes were at first observed; but after a short time, when the renal circulation had been once more established, coagulation necrosis of the renal epithelium could be observed, and this was followed by a deposit of calcareous material. If the ligature were not removed the kidney simply decomposed, but showed no signs of coagulation necrosis or calcification. He accordingly found that something more than the death of the cells was necessary for the production of these changes; that it was necessary for it to occur in living tissue—namely, where the affected cells could obtain a certain supply of blood or lymph.

He considers that the calcification of the necrotic areas is due to the chemical affinity which exists between the necrotic tissue and the calcium salts which are circulating in the blood, probably as a soluble albuminate, which causes them to combine with some of the material of the dead cells and form an insoluble albuminate of lime, which is deposited in them.

Such appears to be the general law governing the production of calcareous deposits—namely, coagulation necrosis of tissue to which some supply of blood or lymph is admitted.

There are, no doubt, subtle differences in the varieties of coagulation necrosis, which occasionally appear to contradict what has just been said. Thus, for example, Kabierski¹⁴ has shown that chromic-acid poisoning will produce coagulation necrosis in rabbit's kidneys which is practically identical with that resulting from anemia and the various agents just enumerated, but calcification fails to follow it.

Can this experimental work be transferred to human pathology, and particularly to the structures under consideration?

Any one who will take the trouble to consider the various varieties of calcific changes in the body will see that conditions more or less similar to those just mentioned precede every variety of calcification, and that it is invariably the sequel of tissue death or necrosis, and is indicative of degeneration and not of a progressive new growth.

It is well known how frequently calcareous changes occur in the uterine fibromata, and there is every reason to suppose that they occur with equal frequency in ovarian fibroids, the difference in the apparent frequency of calcified ovarian and uterine fibroids being due to the great rarity of ovarian fibromata and myo-fibromata and the very frequent occurrence of corresponding growths in the uterus.

It is readily seen that ovarian fibroids present abundant opportunity for calcareous changes, for they are usually quite poorly supplied with blood, and a very slight interference with their circulation could readily suffice for the production of anemic coagulation necrosis with subsequent deposit of calcareous material in the necrosed areas. This mode of origin was observed in the three calcified fibromata of the ovary already described. We are unable to determine the cause of the primary interference with the circulation in these cases; but it is readily seen that the ovary is subjected to a greater extent than most organs to circulatory changes which, under certain circumstances, may lead to the production of necrosis.

A priori one would suppose that the corpus luteum would be particularly prone to calcification, for in its life history the large cells which make up its outer yellow margin undergo hyaline degeneration before entering into the formation of the

transparent corpus fibrosum. Calcareous changes, however, occur but very rarely in it, so we must accordingly suppose that the usual degeneration of the corpus luteum is not of the variety which is most prone to lead to calcification.

Clinical History.—The clinical history of calcified tumors of the ovary does not offer any characteristics which will serve to distinguish this class of tumors from other solid tumors of the ovary, and consequently can be dismissed in a few words. These tumors rarely attain a large size, the largest recorded not exceeding a child's head in size. This is readily understood when we recall the fact that calcification is a sign of degeneration and not of active growth. In two of our cases (2 and 3) there was marked dysmenorrhea, which was due, no doubt, to the pressure exerted by the unyielding calcareous mass upon the nerves in the interior of the ovary. In several cases—our first case and the one reported by Nottingham³¹—there was marked uterine hemorrhage, which ceased entirely after the removal of the growths. The other symptoms of this class of tumors are purely mechanical and are dependent upon the size of the growth, and do not differ in any way from those produced by other solid tumors of the ovary.

Diagnosis.—It is absolutely impossible to diagnose small calcified tumors of the ovary which have not led to considerable increase in its size, and only in rare instances will it be possible to diagnose larger ones from other solid tumors of the uterus or ovary, for on palpation simple fibromata not infrequently feel as hard as if they were calcified.

Treatment.—As the diagnosis of these tumors from other solid tumors of the ovary is practically impossible, one will hardly be called upon to decide as to their treatment; but if by any chance a diagnosis should be made, the removal of the tumor is indicated.

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